

The following Listing of the Claims will replace all prior versions and all prior listings of the claims in the present application:

Listing of The Claims:

1. (Currently Amended) A method of producing a biologically active anti-angiogenic protein, ~~or a biologically active anti-angiogenic mutant, fragment or fusion protein thereof~~, comprising:
  - (a) inserting an isolated polynucleotide sequence encoding a biologically active anti-angiogenic restin protein, ~~or a biologically active anti-angiogenic mutant, fragment or fusion protein thereof~~, into a yeast expression vector, wherein the vector contains a multiple cloning site; and
  - (b) transforming an appropriate yeast strain with the vector of step (a) and maintaining the yeast strain under suitable conditions for the production of the biologically active anti-angiogenic restin protein, ~~or the biologically active anti-angiogenic mutant, fragment or fusion protein thereof~~;thereby producing a biologically active anti-angiogenic restin protein, ~~or biologically active anti-angiogenic mutant, fragment or fusion protein thereof~~.
2. (Original) The method of Claim 1 wherein the yeast strain is *Pichia pastoris*.
3. (Original) The method of Claim 1 wherein the expression vector comprises the pPICZaA vector.
4. (Previously Amended) The method of Claim 1 wherein the biological activity is evaluated by one or more of the following assays: endothelial cell migration, inhibition of
5. (Canceled)

6. (Currently Amended) The method of Claim 1 wherein the biologically active anti-angiogenic restin protein, ~~or biologically active anti-angiogenic mutant, fragment or fusion protein thereof~~ is produced at a concentration of 10-20 milligrams or more per liter of culture fluid.
7. (Canceled)
8. (Currently Amended) The method of Claim 1 wherein the isolated polynucleotide of step (a) additionally comprises a polynucleotide linker, and the biologically active anti-angiogenic restin protein, ~~or biologically active anti-angiogenic mutant, fragment or fusion protein thereof~~ produced in step (b) additionally comprises at least one amino acid residue resulting from the polynucleotide linker.
9. (Currently Amended) The method of Claim 8 wherein the biologically active anti-angiogenic restin protein, ~~or biologically active anti-angiogenic mutant, fragment or fusion protein thereof~~ produced comprises two additional amino-terminus amino acid residues.

Claims 10-13 canceled

14. (Currently Amended) The method of Claim 1 wherein the vector of step (a) comprises a pPICZaA plasmid wherein the plasmid contains a multiple cloning site, said cloning site comprising a His.Tag motif and wherein the biologically active anti-angiogenic restin protein, ~~or biologically active anti-angiogenic mutant, fragment or fusion protein thereof~~ produced in step (b) comprises a histidine tag motif.
15. (Original) The method of Claim 14 wherein the yeast strain is *Pichia pastoris*.

a mammals, arrest of endothelial cells in G<sub>1</sub> phase of the cell cycle, or induction of apoptosis in endothelial cells.

17. (Currently Amended) The method of Claim 14 wherein the biologically active anti-angiogenic restin protein, ~~or biologically active anti-angiogenic mutant, fragment or fusion protein thereof~~ is produced at a concentration of 10-20 milligrams or more per liter of culture fluid.

Claims 18-21 canceled

22. (Currently Amended) A method of producing a biologically active anti-angiogenic restin protein, ~~or a biologically active anti-angiogenic mutant, fragment, or fusion protein thereof~~, comprising:

- (a) inserting an isolated polynucleotide sequence encoding a biologically active anti-angiogenic restin protein, ~~or a biologically active anti-angiogenic mutant, fragment or fusion protein thereof~~, wherein the polynucleotide additionally comprises a linker, wherein the polynucleotide linker encodes at least one amino acid, into a yeast expression vector comprising a pPICZαA plasmid wherein the plasmid contains a multiple cloning site; and
- (b) transforming a *Pichia pastoris* yeast strain with the vector of step (a) and maintaining the yeast strain under suitable conditions for the production of the biologically active anti-angiogenic restin protein ~~or biologically active anti-angiogenic mutant, fragment or fusion protein thereof~~, comprising at least one amino acid residue resulting from the linker polynucleotide;

thereby producing a biologically active anti-angiogenic restin protein, ~~or a biologically active anti-angiogenic mutant, fragment or fusion protein thereof~~.

23. (Previously Amended) The method of Claim 22 wherein the polynucleotide additionally

25. (Currently Amended) A method of producing a biologically active anti-angiogenic protein, ~~or a biologically active anti-angiogenic mutant, fragment or fusion protein thereof~~, comprising:
- (a) inserting an isolated polynucleotide sequence encoding a biologically active anti-angiogenic restin protein, ~~or a biologically active anti-angiogenic mutant, fragment or fusion protein thereof~~, wherein the polynucleotide additionally comprises a linker and wherein the polynucleotide linker encodes at least one amino acid, into a yeast expression vector comprising a pPIC $\alpha$ A plasmid wherein the plasmid contains a multiple cloning site and wherein the cloning site additionally comprises a histidine tag motif; and
  - (b) transforming a *Pichia pastoris* yeast strain with the vector of step (a) and maintaining the yeast strain under suitable conditions for the production of the biologically active anti-angiogenic restin protein ~~or biologically active anti-angiogenic mutant, fragment or fusion protein thereof~~ comprising at least one amino acid residue resulting from the linker polynucleotide, and wherein the protein ~~or mutant, fragment or fusion protein thereof~~ additionally comprises a histidine tag motif;
- thereby producing a biologically active anti-angiogenic restin protein, ~~or a biologically active anti-angiogenic mutant, fragment or fusion protein thereof~~.
26. (Previously Amended) The method of Claim 25 wherein the polynucleotide additionally encodes angiostatin, endostatin, or mutants, fragments or fusion proteins thereof.

Claims 27-39 canceled

- (a) inserting an isolated polynucleotide sequence encoding a biologically active anti-angiogenic apomigren polypeptide into a yeast expression vector, wherein the vector contains a multiple cloning site; and
- (b) transforming an appropriate yeast strain with the vector of step (a) and maintaining the yeast strain under suitable conditions for the production of the biologically active anti-angiogenic apomigren polypeptide;

thereby producing a biologically active anti-angiogenic apomigren polypeptide.

- 41. (New) The method of Claim 40, wherein the isolated polynucleotide of step (a) additionally comprises a polynucleotide linker, and the biologically active anti-angiogenic apomigren polypeptide produced in step (b) additionally comprises at least one amino acid residue resulting from the polynucleotide linker.
- 42. (New) The method of Claim 40, wherein the biologically active anti-angiogenic apomigren polypeptide comprises two additional amino-terminus amino acid residues.
- 43. (New) The method of Claim 40, wherein the vector of step (a) comprises a pPIC $\alpha$ A plasmid wherein the plasmid contains a multiple cloning site, said cloning site comprising a His.Tag motif and wherein the biologically active anti-angiogenic apomigren polypeptide produced in step (b) comprises a histidine tag motif.
- 44. (New) The method of Claim 40, wherein the biologically active anti-angiogenic apomigren polypeptide comprises amino acids 97-181 of SEQ ID NO:20.
- 45. (New) The method of Claim 40, wherein the yeast strain is *Pichia pastoris*.